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5.60.054

Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	October 29, 2021
Subject:	Lybalvi	**Page:**	1 of 4

Last Review Date: December 8, 2023

Lybalvi

Description

Lybalvi (olanzapine and samidorphan)

Background
Lybalvi is a fixed-dose combination of olanzapine and samidorphan. Olanzapine is an atypical anti-psychotic medication currently used as a single agent for the treatment of schizophrenia and bipolar I disorder. An exact mechanism of action for olanzapine is unknown, but its mixture of affinities for different receptors in the brain (serotonin, dopamine, and histamine) is thought to play role in its efficacy. Olanzapine is also a cause of substantial weight gain in patients treated with it. Samidorphan is a mixed opioid antagonist/ partial agonist included in the drug-product formulation to mitigate this side-effect. Samidorphan's blockade of mu-opioid receptors in the intestinal tract is thought to regulate food intake and promote weight loss (1).

Regulatory Status
FDA-approved indications: Lybalvi is a combination of olanzapine, an atypical antipsychotic, and samidorphan, an opioid antagonist, indicated for the treatment of: (1)

- Schizophrenia in adults
- Bipolar I disorder in adults
    - Acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate
    - Maintenance monotherapy treatment

Lybalvi has a boxed warning regarding the increased risk of death in patients with dementia-related psychosis. Lybalvi is not approved to treat dementia-related psychosis (1).

Lybalvi is contraindicated in patients using opioids, or patients undergoing acute opioid withdrawal. Samidorphan is an opioid antagonist and can precipitate withdrawal in patients who are dependent on opioids. Concurrent use can lead to opioid withdrawal syndrome, and possible hospitalization. Before starting Lybalvi, the manufacturer recommends that there be at least a 7 day opioid-free interval from last use of short-acting opioids and at least a 14 day opioid-free internal from last use of long-acting opioids (1).

Lybalvi should be used with caution in patients with a history of seizures, or other conditions that lower seizure threshold (1).

During studies of Lybalvi, a serious reaction known as drug reaction with eosinophilia and systemic symptoms (DRESS) did occur. Lybalvi should be discontinued in suspected cases of DRESS (1).

The safety and effectiveness of Lybalvi in pediatric patients have not been established (1).

Related policies
Abilify Mycite, Zyprexa Relprevv

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Lybalvi may be considered **medically necessary** if the conditions indicated below are met.

Lybalvi may be considered **investigational** for all other indications.

Prior-Approval Requirements

Patients who have NOT filled an opioid medication in the past 90 days are exempt from these Prior Authorization (PA) requirements.

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Schizophrenia
2. Bipolar I disorder

AND NONE of the following:

1. Concurrent opioid use
    a. At least 7 days from last dose of short-acting opioid
    b. At least 14 days from last dose of long-acting opioid
2. Currently undergoing opioid withdrawal
3. Dementia-related psychosis

AND ALL of the following:

1. Prescriber agrees to discontinue medication if patient requires treatment with an opioid
2. Prescriber agrees to monitor for seizures and drug reaction with eosinophilia and systemic symptoms (DRESS)

Prior–Approval *Renewal* Requirements

Same as above

Policy Guidelines

Patients who have NOT filled an opioid medication in the past 90 days are exempt from these Prior Authorization (PA) requirements.

Pre–PA Allowance

None

Prior–Approval Limits

Quantity 90 tablets per 90 days

Duration 12 months

Prior–Approval *Renewal* Limits

Same as above

Rationale

Summary

Lybalvi is a fixed-dose combination of olanzapine and samidorphan for the treatment of schizophrenia and bipolar I disorder. The combination of an atypical antipsychotic with an opioid antagonist was developed to mitigate the significant weight gain associated with the use of olanzapine. Lybalvi has a boxed warning for the increased risk of mortality in patients with dementia-related psychosis. Lybalvi is not indicated for use in this population. Lybalvi is also contraindicated in patients using opioids or undergoing acute opioid withdrawal. Opioid antagonists can precipitate withdrawal from opioids, possibly leading to hospitalization. As such, the manufacturer recommends patients are opioid free for a specified period depending on the formulation of opioid use (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Lybalvi while maintaining optimal therapeutic outcomes.

References

1. Lybalvi [package insert]. Waltham, MA: Alkermes, Inc.; September 2023.

Policy History

Date	Action
October 2021	Addition to PA
December 2021	Annual review. Added the step out verbiage under Pre-PA quantity limit for consistency.
June 2022	Annual review
June 2023	Annual review. Changed policy number to 5.60.054
September 2023	Annual review
December 2023	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.